ISSN: 0975-766X
CODEN: IJPTFI
Available Online through *Research Article*
www.ijptonline.com

EFFECT OF CALCIUM AND VITAMIN B1 ON THE SEVERITY OF PREMENSTRUAL SYNDROME: A RANDOMIZED CONTROL TRIAL

Soheila Samieipour[1], Elahe Tavassoli[2], Akbar Babaei Heydarabadi[3], Seyede Shahrbanoo Daniali[4], Masoumeh Alidosti[5], Faezeh Kiani*[6], Maryam pakseresht[7]

1. MSc in Biochemistry, Faculty of Alleid Medical Sciences Ilam university of medical sciences.ilam. Iran.
2.Assistant Professor, Department of Public Health, School of Health, Shahrekord University of Medical Sciences, Shahrekord, Iran.
3.Assistant Professor, Department of Public Health, Ahvaz Jundishapur University of Medical Sciences, Ahvaz, Iran.
4. PhD in Health Education and Promotion. Department of Health Education & Health Promotion School of Health, Isfahan University of Medical Sciences Isfahan, Iran.
5.Lecturer, Department of Public Health, Behbahan Faculty of Medical Sciences, Behbahan, Iran.
6.Faculty of Alleid Medical Sciences Ilam university of medical sciences.ilam. Iran.
7. Nursing Ph.D student, Department of Nursing, Faculty of Nursing and Midwifery, Ahvaz Jundishapur University of Medical Sciences, Ahvaz, Iran.
Email: fkiani43@yahoo.com

Received on 06-08-2016 *Accepted on 10-09-2016*

Abstract

Background: Premenstrual syndrome (PMS) is a disorder characterized by Physical and psychological symptoms and often occur between 10 to 14 days prior to menstruation and end shortly after the onset of menstruation. It can negatively affect women's daily activities. Recent studies demonstrate that calcium and vitamin B_1 can reduce the symptoms of PMS. The aim of this study was to compare the effect of calcium, vitamin B_1 and placebo on treatment of PMS in students residing at dormitories of Ilam University of Medical Sciences in 2016.

Materials and Methods: In this four-blind placebo-controlled clinical trial, 264 students with PMS residing at dormitories of Ilam University of Medical Sciences were divided randomly into four groups, 1) received vitamin B_1, 2) received calcium, 3) received vitamin B_1 plus calcium and 4) received placebo. All samples took pills once daily for 2 successive menstrual cycles and completed the questionnaires. The data were analyzed using descriptive statistics, Paired t-test and the independent t-test.

Results: Our results showed that after treatment, severity of PMS symptoms reduced significantly in all groups ($p<0.001$). However, comparison of the severity of PMS symptoms between intervention groups and the placebo group

after intervention revealed that, there was a significant difference in this respect (P < 0. 001). Furthermore, mean reduction of PMS symptoms in Vitamin B_1 plus calcium group was more than other groups.

Conclusion: According to our findings, treatment with vitamin B_1 or calcium reduces the severity PMS symptoms but concurrent use of both vitamin B_1 plus calcium is more effective in reducing PMS symptoms. Therefore, this treatment can be used to reach a major goal of midwifery, by decreasing the severity of PMS symptom.

Key Words: premenstrual syndrome, Thiamine (B1), Calcium Carbonate, female.

Introduction:

Every woman has menstruation for about 30 to 35 years in her life. Premenstrual disorders (PMS) are characterized by a variety of unpleasant somatic and psychological symptoms of varying severity that occur regularly during the luteal phase of the menstrual cycle and resolve during menses and may affect the quality of life (1-4).

The prevalence of PMS in the reproductive age has been estimated to be between10%–90% in relation to the studied population and the type of assessment tool used(5, 6)PMS may be influenced by some factors like age, menstrual cycle characteristics, socioeconomic and educational levels, use of hormonal contraceptives, and lifestyle including diet, habits, and physical activities (7, 8)

A total of 150 PMS symptoms have been identified that the most frequent symptoms include breast tenderness, headache, stomachache, back pain, mood swings, tearfulness, anger, confusion, sleep disorder, social withdrawal, fatigue, clumsiness, tension, anxiety, irritability, depression, food craving, constipation and changes in sexual sensation(9-11). PMS can even cause more serious problems such as marital relation disruption, mother-child problems, social isolation, decreased attention, increased psychosomatic symptoms, and even suicide and legal problems(8).

Approximately, 85-90% of women experience various degrees of these symptoms in reproductive age(8). This syndrome affects women in all countries where PMS has been investigated(12).

Because of the direct costs for the healthcare system and especially the indirect costs through the loss of work productivity, effective treatment is needed(13). The suggested treatments are as follows: pharmacological therapies (such as, antidepressants, anxiolytics, cycle-modifying hormonal agents), nutritional supplements (such as, bromocriptine, vitamin D, calcium, magnesium), natural products (such as, vitexagnuscastus extract, evening primrose oil), lifestyle changes (such as, exercise, following dietary recommendations, relaxation therapy) and cognitive behavioral therapy (14).

Vitamin B_1(Thiamin) is one of the complementary therapies used to treat the PMS. It can be effective in treatment of PMS symptoms such as nausea and vomiting. It can also increase the quality of life and decrease depression, fatigue, dysmenorrhea, muscle cramps, and anxiety through coenzyme functions in the metabolism of carbohydrates and main branch of amino acid that plays an important role in appearance of physical and mental symptoms of PMS (15).

Calcium is one of the other nutritional supplements used to treat the PMS. It may play role in the physical and psychological aspect of PMS(16). Changes in calcium concentration could have stimulatory effects on neuromuscular junctions, irritability, fatigue, anxiety, mood changes, change in appetite, depression and muscle cramps(17). Some studies also revealed that in women with PMS, the levels of calcium and some trace elements in red blood cells were lower than normal women(16).

Previous studies investigated the role of each of these drugs in treatment of PMS; However, regarding the high prevalence of PMS and lack of definitive treatment in this regard in Iran we conducted this study to compare the effect of calcium, vitamin B_1, calcium plus vitamin B_1 and placebo on treatment of the PMS symptoms in students residing at dormitories of Ilam University of Medical Sciences in 2016.

Materials and Methods:

This randomized, four-blind clinical trial was performed on students residing at dormitories of Ilam University of Medical Sciences. The study was confirmed by Ethics Committee of Ilam University of Medical Sciences on 12/09/2015 and was awarded the permission number of ir.medilam.rec.1394.88 and The registered number in Iranian registry of clinical trial is IRCT2016011810333N3. All information about participants was preserved and the results were reported anonymously. All performed tests and services in the study were free and patients were not charged for any of them. After providing the necessary clarifications about this study, all participants were asked to sign the written consent.

The inclusion criteria were the as follows: 18 to 30 years old, having normal BMI, having regular menstrual cycles (3 to 8 days of menstruation between 22 to 35 days), not taking medications such as antidepressants, hormones, contraceptives, vitamins, and herbal medications, not having mental or physical disorder including depressive disorders, anxiety and panic disorders, migraine headache, irritable bowel syndrome, asthma, chronic fatigue syndrome, thyroid and adrenal disorders and disorders included in the differential diagnosis of PMS, not having contraindications to take supplements containing calcium Carbonate or vitamin B and not to undergo surgical operation. The students who had the inclusion

criteria were given the PMS diagnosis questionnaire. They recorded their symptoms on PMS diagnosis questionnaire to confirm having PMS. This questionnaire is taken from study of Bakhshani et al (18).It has been designed with the help of DSM-IV definition of PMDD and existing literature on PMS. The questionnaire consisted two sections: The first part included socio-demographic questions such as age, marital status, and residency condition and the second part included 21 self-reporting items assessing frequency and severity of PMS. The questions on the form addressed the most prevalent symptoms including 11 of psychiatric symptoms and 10 of physical symptoms. The participants were asked to identify symptoms they had experienced during two weeks preceding their menstruation in the past two months. Those who had experienced at least 5 symptoms 7 days before menstruation up to 4 days after menstruation were diagnosed to have PMS. The total sample size is set to N = 500 according to similar studies (19) by considering $\alpha = 0.05$, power 80%, 308 out of the first five hundred students who filled out PMS diagnosis questionnaire, had mild to moderate PMS and were asked to take part in this study, 44 students were reluctant to participate in the study and therefore were excluded, remaining a total of 264 students. Then, they were randomly divided into four groups. There were 66 students in each group. Students in the first group received tablets containing 100 mg of vitamin B_1 (vitamin B_1 tablets were produced by the pharmaceutical company of Tehran Chimi, Iran); those in the second group received tablets containing 500 mg of calcium carbonate (calcium were produced by the pharmaceutical company of Tehran Chimi, Iran). Those in the third group received tablets containing 100 mg of vitamin $B_1$and 500 mg of calcium carbonate and those in the fourth group received a placebo. tablets containing placebo were made by 1(gr) food starch. All tablets were given to the participants while they were unaware of the content of the tablets. All participants took tablets once daily during one week before menstruation to 4 days after menstruation for the 2 successive cycles and, concurrently, completed the questionnaires to evaluate changes in the intensity of their symptoms. The questionnaires were collected at the end of 2 cycles and data were analyzed using $SPSS_{16}$ software. We used the Paired t-test to compare changes in the severity of PMS symptoms in each group before and after the intervention and the independent t-test was used to compare changes in the severity of PMS symptoms between groups. $P < 0.05$ was considered statically significant.

Results:

264 out of 308 students screened primarily and had moderate and sever form of PMS were divided into four groups, 66 students received vitamin B_1, 66 students received calcium carbonate, 66 students received vitamin B_1plus calcium

carbonate and 66 students received placebo. Twenty-five participants dropped out during the two month of the intervention. Therefore, the final analysis was performed on 239 samples (Figure 1).

The mean age of participants was 20.32± 8.92 years (range, 18–25 years), BMI was 22.1± 8.92, the mean number of days of the menstrual cycle was 28.41± 3.04 and the mean number of days in period was 6.38± 3.05. Majority of participants were single (89.53%). All participants had similar Socio- demographic and psychometric status.

Before treatment, the symptoms of PMS were mainly in the severe range in each group. As it is shown before the treatment, there was no difference in symptoms between groups and all groups were matched in this regard (Table 1). The average severity of symptoms in each group was compared to placebo group before the treatment, and their homogeneity was proved. According to the results of independent t-test, before the treatment, there was no significant difference in PMS symptoms between placebo group and other groups($P > 0.05$)(Table 2). Table 1 presents the average severity of PMS symptoms before and after intervention in each group. There was a significant difference between the average severity of PMS of symptoms before and after intervention in each group ($P<0.05$). In all groups, the severity of PMS symptoms reduced significantly after treatment ($p<.001$). However, the symptoms of PMS were mainly moderate in vitamin B_1, calcium carbonate and vitamin B_1 plus calcium groups after treatment; but the symptoms were still in the severe range in the placebo group.

1. Table1.The comparison of the PMS symptoms before and after intervention.

Groups	**Before intervention**	**After intervention**	**Difference of means**	**P-value**
Groups	**Before intervention**	**After intervention**	**Difference of means**	**P-value**
Vitamin B1	61.22±30.51	45.91±13.36	19.63±21.82	<0.001
Calcium	61.2±31.4	39.9±11.14	31.89±20.11	<0.001
Vitamin B1 plus Calcium	62.04±30.53	25.31±16.83	41.72±23.81	<0.001
Placebo	61.02±30.52	53.91±18.31	11.52±30.61	<0.001

[a]Values are given as mean±SD, statistical significance assessed using the Paired t-test.

Table2. The comparison of symptoms of PMS between three groups and the placebo group

Symptoms of PMS	**Groups**		**P-value**
	Vitamin B1	**Placebo**	
Before treatment	61.22±30.51	61.02±30.52	>0.05
After treatment	45.91±13.36	53.91±18.31	<0.001
	Calcium	**Placebo**	
Before treatment	61.2±31.4	61.02±30.52	>0.05
After treatment	39.9±11.14	53.91±18.31	<0.001
	Vitamin B1 plus Calcium	**Placebo**	
Before treatment	62.04±30.53	61.02±30.52	>0.05
After treatment	25.31±16.83	53.91±18.31	<0.001

Data are presented as mean±SD, statistical significance assessed using the Independent t-test.

Effect of treatments on the average of severity of PMS symptoms is shown in Table 2. The average of symptoms severity in each group was compared to placebo group after intervention, and their homogeneity was proved. Our results showed that, there was a significant difference between the average PMS symptoms in vitamin B_1 and the placebo group after intervention. Vitamin B_1 decreased the symptoms significantly more than placebo ($P < 0.0001$).

there was a significant difference between calcium group and the placebo group in comparison of the average PMS symptoms after intervention revealed in this case ($P< 0.0001$). Furthermore, Calcium decreased the symptoms more than vitamin B_1. A significant difference was also observed in symptoms of PMS between vitamin B_1 plus calcium group and the placebo group after intervention ($P < 0.0001$). It was observed that the mean reduction of symptoms of PMS in Vitamin B_1 plus calcium group was more than other groups (Table 1). The mean reduction of symptoms of PMS in groups was as follows:

Vitamin B_1 plus calcium >Calcium >Vitamin B_1>Placebo

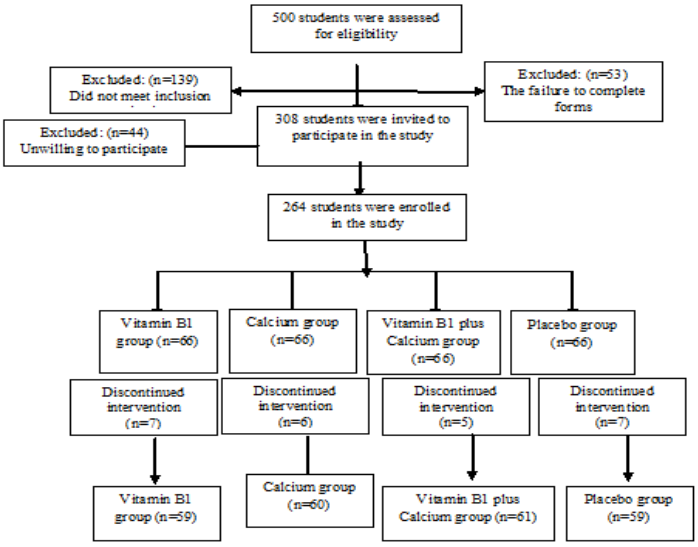

Figure-I.

Discussions:

Premenstrual syndrome is one of the most prevalent causes of women's referral to physicians. In the present study, we compared the effect of calcium and vitamin B_1 on treatment of the PMS symptoms. The reasons for using vitamin B_1 and Calcium in our study were the efficiency, safety and inexpensiveness of these products. We developed a standardized intervention which all participants had to pass through. However, they differed in the severity of PMS symptoms and their need for treatment (20).To our knowledge, a standardized approach for treating PMS does not yet exist. According to what was said, our aim is now to find one effective intervention on treatment of the PMS symptoms. According to the survey of the existing literature on the effect of treatment with supplements in reducing symptoms of premenstrual syndrome, it should be mentioned that there are many confounding variables that can affect the findings. These variables include age, education, socioeconomic status, place of residence and the amount of stress. We minimized the influence of these variables by conducting a randomized, four -blind study among dormitory residents (all participants were matched according to the age, education, living place and life style); removing students using daily nutritional supplements and having a courier to hand over the packaged pills to the participants. Benefits and limitations of this study were discussed above.

Our results showed that before intervention, the severity of the PMS symptoms was clinically similar in all groups, and all were in the severe to moderate range (Table 1). At the end of intervention, the comparison of variations in severity of symptoms before and after intervention revealed that, the average of symptoms of PMS decreased significantly in all groups ($P<0.05$). However, there was a significant difference in severity of PMS symptoms between each intervention group and the placebo group after intervention ($P < 0.001$). Therefore, vitamin B_1, calcium and vitamin B_1 plus calcium were more effective than placebo. Furthermore, vitamin B_1B 1 plus calcium was more effective than other supplements in reducing symptoms of PMS. To our knowledge, this was the first study to examine the effect of calcium plus vitamin B_1in the treatment of PMS symptoms. Therefore, comparing results of this study with those of other studies was limited.

Results of Khajehei et al.'s study (17) also showed that simultaneous consumption of calcium and vitamin D was more effective than placebo ($P<0.05$). Our results confirm those of previous studies regarding the positive effect of vitamin B_1 supplementation on premenstrual symptoms. The results of Abdollahifard et al.'s study showed that vitamin B_1 reduces mental, physical and overall severity of symptoms of PMS (15). The result of Zafari et al is consists with our study too

(21).In the prospective study, Bertone-Johnson (22)et al found that high intakes of vitamin B_1 from food sources were associated with a significantly lower incidence of PMS. Some of other studies showed that vitamin B_1 was effective in increasing the quality of life; releasing energy, reducing skeletal muscle cramps, promoting perfusion to the heart, kidneys, liver, and brain, improving digestion and metabolism of carbohydrates and aminoacids and consequently, decreasing physical and psychological symptoms of PMS such as pain, fatigue, depression, stress, anxiety, and sleep disorders(23-25)

Vitamin B_1 (thiamine) acts as a coenzyme and reduces symptoms of PMS through affecting the performance of coenzymes in the metabolism of carbohydrates, lipids, protein and main branch of amino acid that plays an important role in appearance of physical and psychological symptoms of PMS(15, 26) It affects the function of cardiovascular system, the urinary tract, blood circulation, neurological system. It is also effective in treatment of psychological symptoms of PMS such as depression, fatigue, and anxiety through affecting the brain, increasing endorphin secretion and subsequently causing relaxation and stimulating sleeping(15). Our results also confirm those of previous studies regarding the positive effect of calcium supplementation on premenstrual symptoms. Thys-Jacobs et al. (27) conducted a double-blind clinical trial involving 466 women diagnosed with moderate to severe PMS. In this study, improvements in physical and psychological symptoms were observed in 48% of women who used calcium supplements, compared with only 30% in the placebo group ($P < .001$). Some studies confirmed that intake of calcium carbonate was associated with reduction in symptoms of PMS(24, 25, 27). Penland and Johnson (28) showed that calcium supplements decreased psychological symptoms related to PMS ($p < 0.01$). Ghanbari et al.'s study(16) revealed that PMS symptoms such as early tiredness, appetite changes and depression were reduced significantly more in the women receiving calcium than in those receiving placebo too. Changes in intracellular and extracellular calcium concentration could have stimulatory affect the neuromuscular junctions and psychological symptoms of PMS(29, 30) .The study by Akhlaghi et al. (31) showed a 62% reduction in psychological symptoms and 61% reduction in physical symptoms after treatment with calcium. Shamberger revealed that in women with PMS, levels of calcium in red blood cells were lower than normal (32).

In our study, a high proportion of women responded to placebo, which makes it difficult to establish the actual efficacy of any active treatment. This problem has been observed in other similar studies(29, 33). It appears that receiving attention could positively affect the mental status of participants and cause the treatment of premenstrual syndrome. In this study,

there were no statistically significant differences between groups regarding reported adverse effects. This study, suggests that treatment with calcium, vitamin B_1, especially vitamin B_1 plus calcium is a safe, inexpensive, effective and convenient method for reducing the intensity and frequency of PMS symptoms. With these drugs a lot of physical problems, stress and behavior conflict in everyday life can be prevented. Due to the importance of PMS in the overall quality of life of women, this result can be considered important. Given the study methodology, large sample size, and the treatment effect, these findings provide good evidence about the effectiveness of calcium, vitamin B_1 and especially vitamin B_1 plus calcium as a treatment for PMS. Therefore, it is recommended to be used as first-line treatment for PMS.

Conclusion

This study, which was performed for the first time in Iran, revealed that using vitamin B_1 plus calcium in luteal phase could reduce overall severity of PMS symptoms needless of using it in the entire menstrual cycle. Additional studies are recommended to confirm these findings and to obtain enough evidence for treatment with vitamin B_1 plus calcium as a safe and effective medication for patients who do not desire to or cannot undergo other treatments.

Acknowledgements

Hereby, the researcher appreciates the student deputy and president of Ilam University of Medical Sciences for their contribution and also the students participating in this study. We thank the Deputy for Research of Ilam University of Medical Sciences for the financial support of this study.

References:

1. Yonkers KA, O'Brien PMS, Eriksson E. Premenstrual syndrome. The Lancet.2008;371(9619):1200-10.
2. Hartlage SA, Freels S, Gotman N, Yonkers K. Criteria for premenstrual dysphoric disorder: secondary analyses of relevant data sets. Arch Gen Psychiatry. 2012;69(3):300-5.
3. Soydas EA, Albayrak Y, Sahin B. Increased Childhood Abuse in Patients With Premenstrual Dysphoric Disorder in a Turkish Sample: A Cross-Sectional Study. Prim Care Companion CNS Disord. 2014;16(4).
4. Gillings MR. Were there evolutionary advantages to premenstrual syndrome? EVA Evolutionary Applications. 2014;7(8):897-904.
5. Nisar N, Zehra N, Haider G, Munir AA, Sohoo NA. Frequency, intensity and impact of premenstrual syndrome in medical students. J Coll Physicians Surg Pak. 2008;18(8):481-4.

6. Tschudin S, Bertea PC, Zemp E. Prevalence and predictors of premenstrual syndrome and premenstrual dysphoric disorder in a population-based sample. Arch Womens Ment Health. 2010;13(6):485-94.
7. Ray S, Mishra SK, Roy AG, Das BM. Menstrual characteristics: a study of the adolescents of rural and urban West Bengal, India. Ann Hum Biol. 2010;37(5):668-81.
8. Fard SA, Heshmat R, Majd H. The effect of foot reflexology on premenstrual syndrome. Arch Des Sci. 2012;65(11):140-9.
9. Allais G, Acuto G, Benedetto C, D'Andrea G, Grazzi L, Manzoni GC, et al. Evolution of migraine-associated symptoms in menstrually related migraine following symptomatic treatment with almotriptan. Neurol Sci. 2010;31(1):115-9.
10. Gehlert S, Song I, Chang C-H, Hartlage S. The prevalence of premenstrual dysphoric disorder in a randomly selected group of urban and rural women. Psychol Med. 2009;39(01):129-36.
11. Tacani PM, de Oliveira Ribeiro D, Guimarães BEB, Machado AFP, Tacani RE. characterization of symptoms and edema distribution in premenstrual syndrome. Int J Womens Health. 2015;7:297.
12. Epperson CN, Steiner M, Hartlage SA, Eriksson E, Schmidt PJ, Jones I, et al. Premenstrual dysphoric disorder: evidence for a new category for DSM-5. Am J Psychiatry. 2012;169(5):465-75.
13. Rapkin AJ, Winer SA. Premenstrual syndrome and premenstrual dysphoric disorder: quality of life and burden of illness. Expert Rev Pharmacoecon Outcomes Res. 2009;9(2):157-70.
14. Kues JN, Janda C, Kleinstäuber M, Weise C. Internet-based cognitive behavioural self-help for premenstrual syndrome: study protocol for a randomised controlled trial. Trials. 2014;15(1):1.
15. Abdollahifard S, Koshkaki AR, Moazamiyanfar R. The effects of vitamin B1 on ameliorating the premenstrual syndrome symptoms. Global journal of health science. 2014;6(6):144.
16. Ghanbari Z, Haghollahi F, Shariat M, Foroshani AR, Ashrafi M. Effects of calcium supplement therapy in women with premenstrual syndrome. Taiwan J Obstet Gynecol. 2009;48(2):124-9.
17. Khajehei M, Abdali K, Parsanezhad ME, Tabatabaee HR. Effect of treatment with dydrogesterone or calcium plus vitamin D on the severity of premenstrual syndrome. International Journal of Gynecology & Obstetrics. 2009;105(2):158-61.

18. Bakhshani N, Hasanzadeh Z, Raghibi M. Prevalence of premenstrual symptoms and premenstrual dysphoric disorder among adolescents students of Zahedan. Zahedan Journal of Research in Medical Sciences. 2012;13(8):29-34.
19. Chow S-C, Shao J, Wang H. Sample size calculations in clinical research. Boca Raton: Chapman & Hall/CRC; 2008.
20. Kleinstäuber M, Witthöft M, Hiller W. Cognitive-behavioral and pharmacological interventions for premenstrual syndrome or premenstrual dysphoric disorder: a meta-analysis. J Clin Psychol Med Settings. 2012;19(3):308-19.
21. Zafari M, Behmanesh F, Agha Mohammadi A. Comparison of the effect of fish oil and ibuprofen on treatment of severe pain in primary dysmenorrhea. Caspian J Intern Med. 2011;2(3):279-82.
22. Bertone-Johnson ER, Hankinson SE, Johnson SR, Manson JE. Timing of alcohol use and the incidence of premenstrual syndrome and probable premenstrual dysphoric disorder. J Womens Health. 2009;18(12):1945-53.
23. Gerrits J, Eidhof H, Brunnekreeft J, Hessels J. [9] Determination of thiamin and thiamin phosphates in whole blood by reversed-phase liquid chromatography with precolumn derivatization. Methods Enzymol. 1997;279:74-82.
24. Bertone-Johnson ER, Hankinson SE, Bendich A, Johnson SR, Willett WC, Manson JE. Calcium and vitamin D intake and risk of incident premenstrual syndrome. Arch Intern Med. 2005;165(11):1246-52.
25. Bendich A. The potential for dietary supplements to reduce premenstrual syndrome (PMS) symptoms. J Am Coll Nutr. 2000;19(1):3-12.
26. Hinton DA, Greene JJ. Dietary supplements and food products for treating symptoms of PMS. Google Patents; 2001.
27. Thys-Jacobs S, Starkey P, Bernstein D, Tian J, Group PSS. Calcium carbonate and the premenstrual syndrome: effects on premenstrual and menstrual symptoms. Am J Obstet Gynecol. 1998;179(2):444-52.
28. Penland JG, Johnson PE. Dietary calcium and manganese effects on menstrual cycle symptoms. Am J Obstet Gynecol. 1993;168(5):1417-23.
29. Rapkin A. A review of treatment of premenstrual syndrome & premenstrual dysphoric disorder. Psychoneuroendocrinology. 2003;28:39-53.
30. Rapkin A, Mikacich J. Premenstrual syndrome in adolescents: diagnosis and treatment. Pediatr Endocrinol Rev. 2006;3:132-7.
31. Akhlaghi F, Hamedi A, Javadi Z, Hosseinipoor F. Effects of Calcium supplementation on premenstrual syndrome. Razi Journal of Medical Sciences. 2004;10(37):669-75.

32. Shamberger RJ. Calcium, magnesium, and other elements in the red blood cells and hair of normals and patients with premenstrual syndrome. Biol Trace Elem Res. 2003;94(2):123-9.

33. Dennerstein L, Morse C, Gotts G, Brown J, Smith M, Oats J, et al. Treatment of premenstrual syndrome: a double-blind trial of dydrogesterone. J Affect Disord. 1986;11(3):199-205.

Corresponding Author:

Faezeh Kiani*,

Email: fkiani43@yahoo.com